Antimicrobial Resistance

To the Editor: Davis et al. offered four reasons why local antimicrobial selection pressure in cattle may not play an important role in the dissemination of multidrug-resistant *Salmonella* from cattle to humans (1). Their conclusions differ from those of other recent studies (2-6).

The authors' first two arguments relate to the high levels of chloramphenicol resistance in the United States, despite a relative lack of chloramphenicol use in livestock. In industrialized countries, chloramphenicol use in humans is also low because of medical and legal concerns about aplastic anemia. In Australia, the total average annual human use of chloramphenicol from 1992 to 1997 was 208 kg (6). This is lower than the annual use for most other antibiotics (e.g., sulphonamide 22,331 kg in humans and 24,869 kg in animals; tetracycline 12,677 kg in humans and 77,619 kg in animals) (6). Despite this low use in humans, chloramphenicol resistance can be common in many human pathogens, e.g., multidrug-resistant *Staphylococcus aureus* (7) and *Pneumococcus* (8). Even though tetracyclines are not used in children, children's pneumococcal isolates are often tetracycline resistant (8). With these bacteria, the use of other antibiotics (e.g., penicillins, macrolides, and cephalosporins) appears to drive chloramphenicol (and other) resistance, which is often a part of gene clusters that encode for multidrug resistance. The situation in animals for *Salmonella* is likely to be similar. In the United States, chloramphenicol resistance is higher in isolates from cattle (73% in 1995-97) than from humans (47% in 1997). Therefore, chloramphenicol resistance seen in cattle isolates is very unlikely to have come from the human use of chloramphenicol. Also, chloramphenicol-resistant isolates increased suddenly in both human and animal isolates just after 1990; resistance in cattle isolates rose from 2% to 62% (1). These points suggest that just after 1990 the same chloramphenicol-resistant strains (presumably new clones) were being shared rapidly between cattle and people. This spread is very unlikely to be from people to cattle but rather to people from cattle through food.

The third argument by Davis et al. relates to the spread of resistant strains by wildlife. Even though these strains can move easily around the world, they need to be amplified to cause a serious problem. One of the best ways to amplify resistant bacteria is to give them a selective advantage (e.g., when *Salmonella* is ingested in feed or water by animals that receive in-feed antibiotics).

The authors' fourth argument is that there is still broad dissemination of antibiotic-susceptible strains. So what? In hospitals, despite the overuse of antibiotics, we still see cross-infection with relatively sensitive strains of *S. aureus*, even when these hospitals have a high incidence of multidrug-resistant *S. aureus*. This does not mean that antibiotic use in humans is not one of the important factors in the amplification and spread of multidrug-resistant *S. aureus*.

As Davis et al. point out, antibiotic-resistant bacteria spread worldwide in many ways, including by wild animals and human travel. We need to prevent this spread; however, the central issue is antibiotic use in animals and how it amplifies resistant bacteria (e.g., *Salmonella enterica* serovar Typhimurium DT104). For every antibiotic Davis et al. tested, the level of resistance was higher in *Salmonella* isolates from cattle than from humans (1). The figures supplied by the authors clearly show that antibiotic resistance in cattle and human isolates is related and that resistance in *Salmonella* is and has been more of a problem in cattle than in humans, presumably as a result of widespread use of antibiotics in cattle.

Antibiotic resistance over the medium- to long-term is an inevitable consequence of antibiotic use. Ciprofloxacin and similar fluoroquinolones are the most effective drugs for treating many serious infections in humans, including some *Salmonella* infections (such as bacteremia or osteomyelitis). The prevalence of resistance to fluoroquinolones in human infections acquired from animals through the food chain is increasing (2,4). We should therefore avoid entirely the use of "last-line" human antibiotics such as fluoroquinolones (i.e., antibiotics for which there may be no alternatives if resistance develops) in livestock. All other antibiotics should be used only when there is no other way to prevent or treat infections.

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